

Early Diagnosis of Gall Bladder Cancer: An Appeal

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Abstract



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A team of gastroenterologists, oncologists, pathologists, radiologists, and surgeons from a university teaching hospital in western India make an appeal, through the Journal, to the statutory bodies and the scientific societies related to surgery, oncology, gastroenterology, radiology, and pathology for considering measures, which, if implemented, can help in early diagnosis of gallbladder cancer, the most common nongender organ cancer in women in some parts of India.

Keywords

- ▶ cholecystectomy
- ▶ gallbladder cancer
- ▶ gallstones
- ▶ incidental gallbladder cancer
- ▶ preventive cholecystectomy

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Gallbladder cancer (GBC) is an “Indian” cancer as it is uncommon in the West.¹ The incidence rates of GBC in North India (age-adjusted rate of 11.6 per 100,000 population in Delhi) are one of the highest anywhere in the world; GBC is the most common nongender organ cancer in women in North India (Population-Based Cancer Registry).² Prognosis of clinically obvious GBC is very poor as it is usually diagnosed in advanced stages. An Indian Buddhist middle path of management of GBC, that is, aggressive surgical approach for early GBC and palliative nonsurgical approach for advanced GBC has been advocated.³ Early GBC is usually suspected on imaging or detected on histopathological examination of a gallbladder (GB) removed with a preoperative diagnosis of gallstones (GS)—incidental GBC.⁴

We are a group of gastroenterologists, oncologists, pathologists, radiologists, and surgeons from a university teaching hospital in western India where GBC is a common cancer in women.⁵ During our clinical practice, we have made some observations and identified some problems related to GBC. There is, however, very little and very weak evidence to provide solutions to these problems. Guided by the logic based on our large cumulative experience, we would like to make some suggestions, which are likely to yield benefits in survival of patients with GBC.

1.

Fact: Normal thickness of the GB wall is ≤ 3 mm; > 3 mm is thick-walled GB (TWGB).⁶ TWGB is usually inflammatory but can be malignant.⁷

Observation: In the ultrasonography (US) report, many radiologists/sonologists look at/report on the presence/absence and number and size of the GS only and do not look at/report about the GB wall.

Problem: TWGB is not diagnosed.

Suggestion: A gallbladder reporting and data system (GB-RADS), including the thickness of the GB wall, has been published⁸ and is being validated⁹; radiology societies should discuss and arrive at a consensus whether GB-RADS should be followed by all radiologists/sonologists.

2.

Fact: TWGB on US raises/increases the suspicion of GBC; TWGB is more likely to be GBC than a normal-walled GB.¹⁰ The incidence of GBC in TWGB was 3.3%⁷—higher than a normal (thin)-walled GB. However, US alone is not adequate for proper and complete evaluation of the GB wall for suspicion/diagnosis of GBC.

Observation: Many patients with TWGB on US are not further investigated by the physician/surgeon and are taken up directly for surgery and undergo simple cholecystectomy alone.

Problem: The standard surgical procedure for GBC is extended (radical) cholecystectomy. In case the TWGB turns out to be GBC, simple cholecystectomy will violate the principles of oncological surgery. It then also mandates a second operation for completion extended cholecystectomy which is sometimes refused by the patient.

Suggestion: All patients with TWGB on US should be evaluated further with computerized tomography (CT)/magnetic resonance imaging (MRI) to rule out/suspect GBC.¹¹ The increased yield of diagnosis of GBC by CT/MRI as compared with US alone should then be evaluated in prospective studies. Extended cholecystectomy should be performed if GBC is suspected, that is, in presence of a focal, nonuniform, irregular TWGB (Agarwal 2006). The proportion of patients who are finally found to have benign disease, for example, chronic cholecystitis (CC) or xanthogranulomatous cholecystitis, after undergoing extended cholecystectomy needs to be determined. TWGB with a low suspicion of GBC, that is, uniform, diffuse, regular TWGB should be subjected to anticipatory extended cholecystectomy (AEC), that is, removal of the GB with a small (~ 1 cm) wedge of the liver and frozen section for histopathological examination.¹² The proportion of patients who are finally found to have malignant disease, that is, GBC after undergoing AEC, needs to be determined.

Expected benefit: More cases of GBC will be suspected/diagnosed preoperatively and will receive appropriate surgical management, that is, extended cholecystectomy.

3.

Fact: Incidental GBC is GBC which is not suspected either clinically or on imaging or in the GB specimen and which is detected for first time on the histopathological examination of the GB removed with a preoperative diagnosis of GS.

Observation: Many a time, a grossly normal looking GB removed for GS is not sent for histopathological examination and the specimen is discarded by the surgeon after showing it to the relatives.

Problem: An incidental GBC is missed.

Suggestion: Every removed GB, even if it appears grossly normal, must be sent by the surgeon for histopathological examination to detect an incidental GBC. **Expected benefit:** Incidental GBC, which has a better outcome, will be diagnosed.

4.

Observation: Even when the GB is sent by the surgeon for histopathological examination, sometimes, when the GB specimen looks grossly normal to the pathologist, proper histopathological examination is not done and a routine report of CC is given.

Problem: An incidental GBC is missed.

Suggestion: Every GB specimen, even if it appears grossly normal, must be subjected by the pathologist to proper histopathological examination to detect an incidental GBC.¹¹ The Americas Hepato-Pancreato-Biliary Association recommends that in areas with high GBC prevalence (e.g., India), in GBs that appear normal on gross examination, a minimum of three random areas should be submitted for microscopic assessment.¹³

Expected benefit: Incidental GBC will be diagnosed.

5.

Fact: As a routine, a single longitudinal (“diagnostic”) section of the whole GB, that is, the fundus, body, and neck, is taken for histopathological examination in a grossly normal looking GB removed for GS.¹⁴

Problem: Many cases of incidental GBC are missed. There is no/very little/very poor data available about the incidence of incidental GBC in India.

Suggestion: GB which is removed for GS should be subjected to detailed histopathological examination with multiple; detection of early neoplastic and preneoplastic changes requires “total sampling” of the GB.¹⁴ Pathologists need to conduct prospective studies to find out the increased yield of incidental GBC after “total sampling” of the GB as compared with a single longitudinal (“diagnostic”) section of the whole GB.

Histopathological examination of the GB should be centralized to identified/approved pathology departments which agree to maintain and provide records, and to preserve and provide the paraffin blocks and slides for review, if required.

Expected benefit: The true incidence of incidental GBC in India will be known. A biobank of early GBC tissue will be established.

6.

Fact: Incidental GBC is usually in the early stages as compared with nonincidental (i.e., preoperatively diagnosed) GBC. If treated in time and appropriately, the prognosis of incidental GBC is good and long-term survival, and even cure, is possible. Delay in the management of incidental GBC adversely affects its otherwise good outcome.

Observation: The GB is sent for histopathological examination, which is done and an incidental GBC is detected but, unfortunately, the surgeon/patient do not come to know about the diagnosis due to the report not received or reviewed by the surgeon or due to the lack of communication between the pathologist, surgeon, and/or the patient.

Problem: Management of incidental GBC gets delayed, thus denying the patient a possible chance of cure.

Suggestion: Incidental GBC should be made a notifiable disease—it should be reported (by email, message, and phone call) by the pathologist to the surgeon and by the surgeon to the patient, as soon as possible but definitely within 14 to 28 days of the receipt of the GB specimen in the laboratory/receipt of the report by the surgeon, respectively.

Expected benefit: Patients with incidental GBC will receive timely management resulting in better survival. A registry of incidental GBC will be established.

7.

Fact: Preventive cholecystectomy is not recommended for silent (asymptomatic) GS.¹⁵ The role and place of

preventive cholecystectomy for asymptomatic GS in a high GBC incidence area such as North India is not known.

Observation: A large number of patients with asymptomatic GS, that is, no biliary colic and no complications of GS, are being operated for cholecystectomy (open or laparoscopic).

Problem: The risk (in terms of postoperative complications, especially bile duct injury, of cholecystectomy) versus the benefit (in terms of finding of an incidental GBC) of this approach is not known.

Suggestion: Patients with asymptomatic GS should be operated at identified/approved surgery departments which agree to maintain and provide records about the postoperative course of these patients and which preserve and agree to send the GB specimens to identified/approved pathology departments (vide supra). These GBs removed for asymptomatic GS should then be subjected to detailed histopathological examination to detect early neoplastic or preneoplastic changes in the GB.

Expected benefit: The risk of GBC in presence of asymptomatic GS and the cost-effectiveness of preventive cholecystectomy for asymptomatic GS will be known.

The Indian Council of Medical Research (ICMR) had published a consensus document for the management of GBC in 2015¹⁶ but it does not seem to have reached the practicing doctors and the prevalent practices seem to be at variance from the suggested recommendations. We urge the ICMR and other statutory bodies and scientific societies related to surgery, oncology, gastroenterology, radiology, and pathology to consider our suggestions and formulate guidelines to make suitable recommendations for clinicians (physicians, surgeons, and oncologists), radiologists, and pathologists in India. This will go a long way in early diagnosis, proper management, and improved survival of GBC, a “bad disease” per se.¹⁷

Conflict of Interest

None declared.

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